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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/087,187	02/28/2002	Martin S. Pavelka JR.	96700/736	1355

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EXAMINER	
MARTINELL, JAMES	
ART UNIT	**PAPER NUMBER**
1631	

DATE MAILED: 05/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/087,187	PAVELKA ET AL.	
	Examiner	Art Unit	
	James Martinell	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 July 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

The disclosure is objected to because of the following informalities.

(a) Nucleic acid sequence without SEQ ID NOs as sequence identifiers appear at page 12, lines 28 and 29 and at page 13, lines 17 and 18. Thus, the application does not comply with 37 CFR § 1.821(d). See MPEP 2422.

Appropriate correction is required.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for *Mycobacterium tuberculosis* comprising a mycobacterial lysA gene containing an unmarked mutation introduced by allelic exchange requiring lysine for growth, does not reasonably provide enablement for all mycobacteria containing an unmarked mutation, vaccines, and methods of treatment or protection. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The application does not enable methods for making and using recombinant slow-growing mycobacteria containing more than one unmarked mutation or from a strain other than *M. tuberculosis* with a lysA mutation. It would require undue experimentation for one of skill in the art to isolate any other unmarked mutants generated by allelic exchange. The application does not enable one of skill in the art to produce a vaccine and use that vaccine to treat or prevent tuberculosis (claims 13-18). Tuberculosis vaccination is a highly unpredictable art, even in the hands of highly skilled artisans. This is evidenced by Guleria et al (Nature Medicine 2(3), 334 (1996)) wherein met1 auxotrophs of BCG for vaccination against *M. tuberculosis* resulted in a lower level of protection than did an inoculation of BCD alone or leucine auxotrophs (*e.g.*, see page 335 and Figure 3). In addition, Roche et al (Trends in

Microbiology 3(10), 397 (1995)) teaches that the efficacy of BCG vaccines for *M. tuberculosis* is highly variable and depends upon various factors associated with the vaccine, such as: the BCG strain, vaccine viability, dose, route of administration, and boosters. Gheorghiu (Int. J. Immunopharmac. 16(5/6), 435 (1994)) teaches that the oral route is more effective than the intradermal route (*e.g.*, see Abstract). Finally, Maes (Medical Hypotheses 53(1), 32 (1999)) outlines difficulties in the production of effective tuberculosis vaccines (*e.g.*, see the Summary section). The instant application does not address these variables in connection with the production and administration of tuberculosis vaccines.

Claims 3-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are vague and indefinite.

(a) The recitation of "structural component or an amino acid" (claim 3) is vague and indefinite because the metes and bounds of the phrase are not clear within the context of the claimed invention.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-17 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No. 6,423,545. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims embrace the claims of the patent. For example, claims 1-6 and 13-17 embrace claims 1, 2, and 7 of the reference; claim 7 embraces claims 3-6 of the reference; claims 8, 11, and 12 embrace claims 8-10 of the reference, claim 9 embraces claim 9 of the reference; and claim 10 embraces claim 10 of the reference.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3, 7-10, 13, and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pelicic et al (FEMS Microbiol. Lett. 144: 161 (1996)) in view of Pelicic et al (U.S. Patent No. 5,843,664). Pelicic et al (1996) teaches a recombinant slow-growing mycobacterium, *M. bovis* BCG, comprising a marked mutation in the ureC gene, and a method of obtaining it through the positive selection of allelic exchange mutants by introducing a suicide plasmid into a mycobacterium comprising a kanamycin resistance selectable marker, a sacB counterselectable marker, and a marked mutation in the mycobacterium ureC gene, selecting primary recombinants incorporating the kanamycin marker, culturing the recombinants, selecting for the secondary recombinants that have lost the sacB marker, and isolating the secondary recombinants containing the unmarked mutant mycobacterial gene (*e.g.*, figure 2, page 163). The reference further discloses that the method may be used with unmarked mutants wherein the antibiotic resistance cassette is replaced by any mutation and suggests the use of the system with other species of *Mycobacterium* (*e.g.*, sections 3.2 and 3.3 and page 165, column 1, first full paragraph). Pelicic et al (1996) does not teach the use of unmarked deletion mutations in the absence of antibiotic

resistance markers in the step. Pelicic et al (U.S. Patent No. 5,843,664) teaches the use of unmarked deletion mutations in *M. smegmatis* in a two step selection method using the sacB counterselectable marker and uracil auxotrophs wherein the second selection process was conducted in the absence of antibiotic resistance markers (*e.g.*, column 7, lines 49-67). It would have been obvious for one of ordinary skill in the art at the time the invention was made to use unmarked deletion mutants as taught in Pelicic et al ('664) in the method of Pelicic et al (1996), the motivation being the teaching in Pelicic et al ('664) at column 7, lines 31-47.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James Martinell whose telephone number is (571) 272-0719. The fax phone number for Examiner Martinell's desktop workstation is (571) 273-0719. The examiner works a flexible schedule and can be reached by phone and voice mail. Alternatively, a request for a return telephone call may be e-mailed to james.martinell@uspto.gov. Since e-mail communications may not be secure, it is suggested that information in such requests be limited to name, phone number, and the best time to return the call.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (571) 272-0722.

PLEASE NOTE THE NEW FAX NUMBER

The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

James Martinell, Ph.D.
Primary Examiner
Art Unit 1631

5/18/04